

## REMARKS

Reconsideration of this application, as amended, is respectfully requested. Claims 39-87 have been cancelled. New claims 88-108 have been inserted. All amendments have been made without prejudice or disclaimer. Applicants reserve the right to prosecute all cancelled or otherwise unclaimed subject matter in this or another application as appropriate. Consideration and entry of this amendment and remarks is respectfully requested.

Applicants thank the Examiner for the discussion of June 10, 2009. New claims 88-105 encompassing a sequestering subunit comprising an opioid antagonist overcoated (e.g., covered) by a composition comprising an opioid agonist have been submitted herewith. The subject matter of claims 88-105 encompasses a sequestered subunit comprising an opioid antagonist (e.g., naltrexone) completely surrounded by a composition comprising an opioid agonist (e.g., morphine). If one tampers with the composition (e.g., by crushing it), the opioid antagonist becomes co-mingled with the opioid agonist, thereby interfering with the effects of the agonist. Applicants do not believe the claimed subject matter is described by or obvious in view of the known prior art.

### Rejections Under 35 U.S.C. § 102(e)

#### A. Breder et al. (US 2003/0157168)

Claims 39-47, 50-58, 61-69, and 82-87 stand rejected under 35 U.S.C. § 102(e) as anticipated by Breder et al. (US 2003/0157168). While Applicants disagree that any of claims 39-47, 50-58, 61-69, or 82-87 are anticipated by Breder, all of those claims have been cancelled for reasons unrelated to the cited art and the rejection is therefore moot. However, Applicants do not believe the subject matter of new claims 88-108 is not anticipated by Breder, as set forth below.

In rejecting claims 39-47, 50-58, 61-69, and 82-87, the Examiner alleged that Breder teaches:

Beads coated with an opioid agonist, and opioid antagonist in non-releasable form . . . at [164] and . . . multiple subunits with releasable therapeutic with a coated (sequestered) antagonist in each....Subunits with either agonist or antagonist are set out at [213].

As discussed in the June 12 teleconference, Applicants do not believe Breder discloses a single subunit coated with both an agonist and an antagonist. As stated at paragraph [164] of Breder:

When a hydrophobic controlled release coating material is used to coat inert pharmaceutical beads such as nu pariel 18/20 beads, which are already coated with an opioid agonist, a plurality of the resultant solid controlled release beads may thereafter be placed in a gelatin capsule with the opioid antagonist in a substantially non-releasable form. (Emphasis added.)

At paragraph [213], Breder refers to:

...melt extruded material...prepared without the inclusion of the opioid agonist and/or opioid antagonist particles, which are added thereafter to the extrudate. Such formulations typically will have the drugs mixed together with the extruded matrix material, and then the mixture would be tableted to provide a slow release of the opioid agonist. (Emphasis added.)

In each of the cited sections, Breder merely describes agonists and antagonists that are prepared as separate subunits and then combined into a single capsule or extrudate. In contrast, the claims 88-105 relate to a sequestered opioid antagonist that is overcoated with a composition comprising an opioid agonist; the antagonist and agonist are part of a single subunit. In addition, it has not been demonstrated that Breder teaches the use of a surfactant in a blocking agent within a sequestering subunit. Accordingly, Applicants respectfully maintain that Breder does not disclose the instantly claimed formulations.

#### B. Oshlack (US 2003/0064099)

Claims 39-47, 50-58, 61-69, and 82-87 stand rejected under 35 U.S.C. § 102(e) as anticipated by Oshlack et al. (US 2003/0064099). While Applicants disagree that any of claims 39-47, 50-58, 61-69, or 82-87 are anticipated by Oshlack, all of those claims have been cancelled for reasons unrelated to the cited art and the rejection is therefore moot. However, Applicants do not believe the subject matter of new claims 88-108 is not anticipated by Oshlack, as set forth below.

In rejecting claims 39-47, 50-58, 61-69, and 82-87, the Examiner alleged that Oshlack teaches:

Beads coated with an opioid agonist, and opioid antagonist in non-releasable form. . .at [0084] and. . .multiple subunits with releasable therapeutic with a coated (sequestered) antagonist in each. Subunits with either agonist or antagonist are set out at this paragraph. A Hydrophilic core, with an aversive agent coating further coated with a hydrophobic agent is listed at [0086].

Paragraph [0084] of Oshlack is reproduced (in part) below:

In certain embodiments of the present invention a hydrophobic material is used to coat inert pharmaceutical beads such as nu pariel 18/20 beads comprising an opioid analgesic, and a plurality of the resultant solid controlled release beads may thereafter be placed in a gelatin capsule. . .The one or more aversive agents may also be coated onto the beads onto the beads comprising the opioid analgesic, may be prepared as separate beads and then combined in a dosage form including the controlled release beads comprising an opioid analgesic, or the one or more aversive agents may be mixed in the dosage form with the controlled release beads comprising the opioid analgesic. (Emphasis added.)

Similarly, at paragraph [0086], Oshlack states:

Spheroids or beads coated with an opioid analgesic are prepared, e.g., by dissolving the opioid analgesic in water and then spraying the solution onto a substrate, for example, nu pariel 18/20 beads, using a Wuster insert. Thereafter, the one or more aversive agent is optionally added to the beads prior to coating. (Emphasis added.)

As discussed in the June 12 teleconference, Oshlack only refers to coating agonist-containing controlled release beads with an aversive agent. In contrast, the claims 88-105 relate to a sequestered opioid antagonist that is overcoated with a composition comprising an opioid agonist. Applicants do not believe Oshlack teaches a single subunit comprising an antagonist coated with a composition comprising an agonist. In addition, it has not been demonstrated that Oshlack teaches the use of a surfactant in a blocking agent in a sequestering subunit. Applicants respectfully maintain that Oshlack does not disclose the instantly claimed compositions.

**Rejections Under 35 U.S.C. § 103(a)**

Claims 15-17 and 38 were rejected in the last Office Action as obvious in view of Breder et al. (US 2003/0157168). Claims 15-17 and 38 were cancelled in the amendment filed Feb. 4, 2008. The rejection as to those claims is therefore moot. Applicants respectfully maintain that Breder does not render new claims 88-108 obvious. It is therefore respectfully requested that these rejections be withdrawn.

**CONCLUSIONS**

Reconsideration of this application, as amended, is respectfully requested. The Examiner is encouraged to contact the undersigned if it is believed doing so would expedite prosecution.

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